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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/580,803	11/24/2006	Shey-Shing Sheu	RO0006US.NP	8858

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EXAMINER

CRANE, LAWRENCE E

ART UNIT	PAPER NUMBER
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1623

NOTIFICATION DATE	DELIVERY MODE
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ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

poreilly@licataandtyrrell.com

Office Action Summary	Application No. 10/580,803	Applicant(s) SHEU ET AL.	
	Examiner Lawrence E. Crane	Art Unit 1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on April 1, 2008 (amendment).
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-12, 14-45 and 55-57 is/are pending in the application.
- 4a) Of the above claim(s) 55-57 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-12 and 14-45 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 01 April 2008 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Claims **13 and 46-54** have been cancelled, claims **1-10, 14-15, 17-24, 27, 28, 30-32, 37 and 44** have been amended, the Abstract, the Figures and the disclosure have been amended as requested, and new claims **55-57** have been added as per the amendment filed April 1, 2008. No additional or supplemental Information Disclosure Statements (IDSs) have been received as of the date of this Office action. A supplemental reference including a few pages from a biochemistry text have been supplied by applicant in support of applicant's arguments in response.

Claims **1-12, 14-45 and 55-57** remain in the case.

Note to applicant: when a rejection refers to a claim **X** at line **y**, the line number "y" is determined from the claim as previously submitted by applicant in the most recent response including ~~lines deleted by line through~~.

Claims **1-12, 14-45 and 55-57** are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabled for making and testing for an anti-oxidant protective effect of a few choline esters of the compounds glutathione, N-acetyl cysteine, and cysteine, does not reasonably provide enablement for the very large number of alternative structures, the biological testing thereof, and all of the alternative syntheses claimed therefore. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The fundamental issue here is whether practicing the full scope of the instant invention is possible without undue experimentation. As provided for in *In re Wands* (858 F.2d 731, 737; 8 USPQ 2d 1400, 1404 (Fed Cir. 1988) the minimum factors to be considered in determination of whether a conclusion of "undue experimentation" is appropriate are as follows:

A. The breadth of the claims: The instant claims are directed to a very large number of compounds the vast majority of which have not been structurally identified, synthesized and/or tested for the capability to inhibit the adverse effects of oxidants on cell functions, with particular emphasis on mitochondrial functions. No claimed compound has been tested to determine activity in the treatment of any specific disease condition.

B. The nature of the invention: This question is dealt with the previous paragraph.

C. The state of the prior art: There is no prior art presently of record disclosing the instant claimed compounds or their administration in the treatment of diseases.

D. The level of one of ordinary skill: The ordinary practitioner would be expected to know how to make and how to test in a preliminary manner the compounds of the instant claims. But in view of the absence of any disclosure of a test regimen involving a test host (e.g. lower mammals, etc.) accepted in the art as predictive of efficacy against a particular disease condition, there is necessarily an extremely high level of skill in determining whether the instant results are extrapolatable to the treatment of actual disease conditions of the kind listed in claim **40** or the effective inhibition of “oxidative stress” the mammalian cell types listed in claims **38 and 45**.

E. The level of predictability in the art: The predictability in the synthetic portion of the instant claims is high in view of the well known methods cited in the instant IDS’s. However, the instant disclosure’s 11th Example is only prospective, and there are therefore no Examples wherein an actual disease condition has been shown to have been effectively treated by administration of any compound disclosed or claimed herein, thereby rendering the instant method of treatment claims directed to subject matter in an area of medical disease treatment that is highly unpredictable due to the meager amount of relevant test data disclosed herein and of test data disclosed in the prior art.

F. The amount of direction provided by the inventor: The instant disclosure discloses how to make a small number of the compounds disclosed and supplies some biological testing data suggesting that cells treated *in vitro* have a longer life span under oxidative stress than control populations. However, the instant disclosure does not provide any test data permitting one of ordinary skill to believably extrapolate from the test data provided to the plethora of diseases listed in claim **40**, diseases some of which are well known to be either incurable including Lou Gehrig’s disease (“amyotrophic lateral sclerosis,” aka ALS) or at best very difficult to effectively treat including “aging-related diseases” generally.

G. The existence of working examples: This subject is dealt with in the previous paragraph.

H. The quantity of experimentation needed to make or use the invention based on the content of the disclosure is deemed to be excessive because the instant disclosure, while enabling the synthesis of a few compounds and providing a showing that oxidative stress induced in cells in culture (in vitro) can be reduced by administration of a few of the compounds prepared, there is insufficient data to provide a reasonable basis for extrapolation of the biological test data provided to any *in vivo* disease treatments.

Applicant's arguments filed April 1, 2008 have been fully considered but they are not persuasive.

Upon review of section "D" above, a minor but important error was discovered. Examiner regrets the error, but notes that the misstatement made was inconsistent with many of the other correct statements. The change asserts that "an extremely high level of skill" is required to extrapolate the instant exemplifications to the treatment of the disease conditions listed in claim **40**. This amended paragraph now clearly supports the conclusion that undue experimentation is essential to the practice of the instant claimed method of treatment.

The instant claims are directed to several different subject matters: i) compounds and pharmaceutical compositions, ii) method of disease treatments, and iii) method of making compounds. The first and third subject matters can be found to be reasonably well enabled for claims **1-12, 14-32 and 55-57** that, following clarifying amendments, are more well defined and have scopes more in line with the examples provided.

In re the second subject matter area, claims **33-45**, applicant is respectfully requested to note the following: *Ex parte Balzarini et al.* 21, USPQ 2d 1892, 1894 (BPAI, 1991) stands in its first opinion for the proposition that claims directed to medicinal treatments of diseases in highly unpredictable art areas are properly rejected under 35 U.S.C. §112, first paragraph as lacking adequate enablement, in the absence of sufficient test data in support of the efficacy of the alleged treatment. See also MPEP at §2107.03. This precedent in examiner's view is more closely on point than the precedents cited by applicant. Applicant has listed a substantial number of diseases in instant claims **39 and 40** none of which have not been specifically shown to be effectively treated by any of the compounds disclosed and specifically listed herein, and which are not otherwise known in the prior art to be treatable by administration of medicinal substances disclosed herein; e.g. neurodegenerative diseases, neuromuscular

degenerative disorders, various developmental delays, ALS, aging related diseases, etc., etc. For these reasons, and for the reasons of record, the method of treatment claims are deemed to lack adequate enabling support.

Examiner notes applicant's amendments and appreciates that the instant claim scope has been somewhat narrowed and definitiveness somewhat improved. However, the problem of excessive scope remains in the area of the breadth of compounds claimed to be medicinally active, and more particularly in the area of the vast array of disease conditions alleged to be effectively treatable when applicant has not provided any test data to enable same. Applicant is respectfully requested to recall *Brenner v. Manson* (148 USPQ 689 (S. Ct. 1966)), a precedent that stands for the proposition that a patent is granted for work already accomplished and “... is not a hunting license.”

Claims **1, 11, 33, 36, 43 and 55** are objected to because of the following informalities:

In claim **1** at line 3, the structure labeled “(I)” and “(II)” are presented as -- cations -- only, not as compounds. Apparently applicant has failed to include the monovalent anionic counter ions (-- X⁻ -- plus a definition thereof?) necessary to meet the minimum definitional requirements of the term “compound” at line 1. See also claims **33 and 55** for the same error in view of dependence from claim **1** and the same error, respectively.

In claim **36**, the last two listed compounds are not correctly named. Applicant is referred to paragraph 0075 wherein the synthesis and a chemical name are disclosed that materially differs from the two chemical names provided at the last four lines of claim **36**. See paragraph 0076, lines 12-13 for a correct chemical name. See also claims **11 and 43** for the same nomenclature errors.

Appropriate correction is required.

Claims **1-11, 31 and 55-57** are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim **1** at line 2, the term “comprising” renders the claim indefinite because said term implies that the remainder of the claim fails to completely define the subject matter; e.g. that

the noted term of art “comprising” implies that the “compound” being defined “includes” undefined structural elements. Examiner respectfully suggests replacement with the above noted term

-- having the structural formulas ... -- or the like as one way to effectively address the instant rejection. See also claims **6-9** wherein the terms “comprising” and “comprises” cause the same problem.

Applicant’s arguments with respect to claims **1-54** have been considered but are moot in view of the new grounds of rejection. This new ground of rejection was necessitated by applicant’s amendments.

In claim **1** at line 5, the terms “amino acid” and “amino acid derivative group having antioxidant activity” are incompletely defined because the structural identity or identities of the “derivatives” and the identity or identities of the functional groups responsible for the “antioxidant activity” have not been defined with particularity; i.e. by identification of specific chemical substituent moieties included, and not included, within the metes and bounds of the claimed subject matter. See also claims **2-9** wherein the same problems reoccur

Applicant’s arguments filed April 1, 2008 have been fully considered but they are not persuasive.

Examiner unwisely stated at the end of the above rejection in the first Office action on the merits that “[t]his rejection does not apply when the preceding terms precede the term ‘group.’” Examiner has reconsidered this overly specific suggestion and retracts same for the following reasons.

While the addition of the term “group” does correct the misapprehension that the claimed compounds include the compounds known as “amino acids” as is, the addition of this term does not correct other problems with the noted terms, including the presence of the included term “having antioxidant activity,” a functional term that apparently refers to the necessity of having -- -SH -- groups present. In addition, the term “peptide” is defined to include “two or more amino acids or amino acid derivatives,” does not include the term -- group -- and does not adequately define the metes and bounds implied by the included term “derivatives.”

In claim **10** the terms in the “Markush group” are each the chemical name of a compound, not the name of a substituent group; e.g. did applicant intend the first term to read in part -- glutamylcysteinyl --? See also claim **11** wherein the first six names appear to have the same problem.

Applicant’s arguments with respect to claims **1-54** have been considered but are moot in view of the new grounds of rejection. This new ground of rejection was necessitated by applicant’s amendments.

In claim **31** at line 4, the term “pyrrolyl” is properly listed in claim **30** because, like the Markush group members in claim **30**, “pyrrolyl” is a heteroaromatic ring substituent and therefore literally cannot accommodate variable “Q².” Examiner respectfully suggests one possible solution: moving the term “pyrrolyl” to claim **30**.

Applicant’s arguments with respect to claims **1-54** have been considered but are moot in view of the new grounds of rejection. This new ground of rejection was necessitated by applicant’s amendments.

In claim **55** the terms “R ” and “R’ ” are not defined as specific chemical structures or even generic chemical structures, nor are the particular protecting group or groups to be removed. Therefore, the noted claim is indefinite for failing to provide sufficient information to permit the ordinary practitioner to determine the particular process step or steps being claimed. The additional details provided in claims **56 and 57** do not make up for the deficiencies of claim **55** thereby rendering all of the claims indefinite.

Applicant’s arguments with respect to claims **1-54** have been considered but are moot in view of the new grounds of rejection. This new ground of rejection was necessitated by applicant’s amendments.

Claims **14-25** are rejected under 35 U.S.C. §112, fourth paragraph, as being of improper dependent form for failing to further limit the subject matter of a previous claim.

Claims **14-25** are dependent from now cancelled claim **13** and therefore are improperly dependent.

Applicant's arguments with respect to claims **1-54** have been considered but are moot in view of the new grounds of rejection. This new ground of rejection was necessitated by applicant's amendments.

The non-statutory double patenting rejection, whether of the obviousness-type or non-obviousness-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornam*, 686 F. 2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir 1985); and *In re Goodman*, 29 USPQ 2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 C.F.R. § 1.321(b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 C.F.R. §1.78(d).

Effective January 1, 1994, a registered attorney or agent or record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 C.F.R. §3.73(b).

Claims **1-12, 14-45 and 55-57** are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims **1-5** of copending Application No. **11/312,873**. Although the conflicting claims are not identical, they are not patentably distinct from each other because the defined amino acid-choline ester derivatives, the pharmaceutical compositions thereof, the method of treatment wherein said amino acid-choline ester derivatives are administered, and the method of making said aminoacids-choline esters, are directed to substantially overlapping subject matter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant's arguments filed April 1, 2008 have been fully considered but they are not persuasive.

Applicant has acknowledged the presence of this rejection, has disagreed with this rejection, but has not supplied a Terminal Disclaimer or an argument in support of said disagreement. Therefore, this rejection has been maintained.

Claims **1-12, 14-45 and 55-57** of this application conflict with claims **1-5** of Application No. **11/312,873**. 37 C.F.R. §1.78(b) provides that when two or more applications filed by the same applicant contain conflicting claims, elimination of such claims from all but one application may be required in the absence of good and sufficient reason for their retention during pendency in more than one application. Applicant is required to either cancel the conflicting claims from all but one application or maintain a clear line of demarcation between the applications. See MPEP §822.

Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL**. Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. §1.136(a).

A shortened statutory period for response to this final action is set to expire **THREE MONTHS** from the date of this action. In the event a first response is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. §1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than **SIX MONTHS** from the date of this final action.

Papers related to this application may be submitted to Group 1600 via facsimile transmission (FAX). The transmission of such papers must conform with the notice published in the Official Gazette (1096 OG 30, November 15, 1989). The telephone number to FAX (unofficially) directly to Examiner's computer is 571-273-0651. The telephone number for sending an Official FAX to the PTO is 571-273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. E. Crane whose telephone number is **571-272-0651**. The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. S. Anna Jiang, can be reached at **571-272-0627**.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is **571-272-1600**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status Information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see < <http://pair-direct.uspto.gov> >. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

/L. E. C./

Patent Examiner, Art Unit 1623

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06/29/2008

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